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**Declaration under Rule 4.17:**

— of inventorship (Rule 4.17(iv)) for US only

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(75) Inventor/Applicant (for US only): SILENCE, Karen [BE/BE]; Jean Tombeurstraat 21, B-3090 Overijse (BE).

(54) Title: RECOMBINANT VHH SINGLE DOMAIN ANTIBODY FROM CAMELIDAE AGAINST VON WILLEBRAND FACTOR (vWF) OR AGAINST COLLAGEN

(57) Abstract: The present invention relates to polypeptides comprising at least one single domain antibody directed against vWF, vWF A1 domain, A1 domain of activated vWF, vWF A3 domain, gpIb and/or collagen, for the treatment for conditions which require a modulation of platelet-mediated aggregation. A further aspect of the invention is methods of production of said polypeptides, methods to coat devices with such polypeptides used in medical procedures (e.g. PCTA, stenting) and kits for the diagnosis of diseases related to platelet-mediated aggregation.

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# INTERNATIONAL SEARCH REPORT

International Application No

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**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 7	C07K16/36	C07K16/18	C12N15/13	A61K39/395	A61K38/49
	A61P7/02	A61M31/00			

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, MEDLINE

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2001/024647 A1 (MCLEOD ANNE ET AL) 27 September 2001 (2001-09-27) paragraph '0013! - paragraph '0025!; claims 1-17 ----- ARBABI GHARROUDI M ET AL: "SELECTION AND IDENTIFICATION OF SINGLE DOMAIN ANTIBODY FRAGMENTS FROM CAMEL HEAVY-CHAIN ANTIBODIES" FEBS LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 414, no. 3, 15 September 1997 (1997-09-15), pages 521-526, XP002069903 ISSN: 0014-5793 page 521, right-hand column, paragraphs 4,5 page 525, right-hand column, paragraph 3 ----- -/-	1-28, 30-32
Y	-----	1-28, 30-32

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the International search

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# INTERNATIONAL SEARCH REPORT

International Application No  
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2002/028204 A1 (KITO MORIKAZU ET AL) 7 March 2002 (2002-03-07) paragraph '0103! - paragraph '0167! -----	1-28, 30-32
Y	MUYLDERMANS S: "SINGLE DOMAIN CAMEL ANTIBODIES: CURRENT STATUS" REVIEWS IN MOLECULAR BIOTECHNOLOGY, ELSEVIER, AMSTERDAM,, NL, vol. 74, no. 4, June 2001 (2001-06), pages 277-302, XP001057480 ISSN: 1389-0352 the whole document -----	1-28, 30-32
Y	US 6 251 393 B1 (MCLEOD ANNE ET AL) 26 June 2001 (2001-06-26) column 3 - column 6 -----	1-28, 30-32
Y	WO 02/057445 A (MURUGANANDAM ARUMUGAM ; STANIMIROVIC DANICA (CA); NARANG SARAH (CA); N) 25 July 2002 (2002-07-25) page 24, line 1 - page 47, line 15 -----	1-28, 30-32
A	CORTEZ-RETAMOZO V ET AL: "Efficient tumor targeting by single-domain antibody fragments of camels" INTERNATIONAL JOURNAL OF CANCER, NEW YORK, NY, US, vol. 98, no. 3, 20 March 2002 (2002-03-20), pages 456-462, XP002248403 ISSN: 0020-7136 page 457, left-hand column, paragraphs 3,4 -----	1-28, 30-32

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International application No.

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**Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)**

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
  - a. type of material
    - a sequence listing
    - table(s) related to the sequence listing
  - b. format of material
    - in written format
    - in computer readable form
  - c. time of filing/furnishing
    - contained in the international application as filed
    - filed together with the international application in computer readable form
    - furnished subsequently to this Authority for the purpose of search
2.  In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

## INTERNATIONAL SEARCH REPORT

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### Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.: 29 because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
  
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 29

Present claim 29 relates to a compound defined by reference to a desirable characteristic or property, namely "that modulates platelet-mediated aggregation identified according to the method of claim 27".

The claims cover any compound having this characteristic or property, whereas the application provides no support within the meaning of Article 6 PCT and no disclosure within the meaning of Article 5 PCT for such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claim also lacks clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, no search has been carried out for this claim.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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Patent document cited in search report	Publication date	Patent family member(s)		Publication date
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